Remarks

Claim 7 stands rejected as indefinite for depending on a cancelled claim. Claim 7 has been amended to depend on claim 1. Accordingly Applicants respectfully request that this rejection be withdrawn.

Claims 1-3 and 5-7 stand provisionally rejected for obviousness-type double patenting over claims 1-11 of co-pending Serial No. 09/817,913. A terminal disclaimer accompanies this reply. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 1-3 and 5-7 stand rejected as obvious over Yoshida *et al.* and others. Applicants respectfully traverse this rejection. According to the Office action, the motivation to combine Yoshida with the other references is that Yoshida taught the need for "the use of a more specific and potent inhibitor of histone deacetylase ... to carry out further more refined analyses." However, this statement was taken out of context. The full quote is:

> Experiments *in vivo* using n-butyrate at a high concentration have to be interpreted with caution because of its pleitropic effects on other enzymes, cytoskeleton, cell membranes, etc. Therefore, the use of a more specific and potent inhibitor of histone deacetylase seems to be necessary to carry out further more refined analyses.

Thus, the technical problem faced by Yoshida was to find a more specific and potent inhibitor of histone deacetylase than n-butyrate, the only previously known inhibitor of histone deacetylase. Yoshida succeeded, solving the problem through the use of (R)-Trichostatin A (TSA). Later, Yoshida continues "TSA thus seems to be a very useful tool for analyzing the multiple functions of histone acetylation in regulatory mechanisms of cell proliferation and differentiation."

At page 17178 Yoshida states:

> The results presented in this paper clearly show that TSA is a potent inhibitor of the mammalian histone deacetylase enzyme. Its extremely low K_i value for the histone deacetylase can fully account for the accumulation of highly acetylated histones by the low concentration of the drug *in vivo*.

Yoshida isn't finished praising TSA. In the following column:

> We confirmed that TSA has no effect on the other enzyme activities such as protein kinases, protein phosphatases, DNA topoisomerases and calmodulin *in vitro*. Therefore, the use of TSA will be expected to be useful in analyzing the biological roles of histone acetylation without giving adverse side effects.

Yoshida concludes the article saying "TSA will be an important tool in the analysis of the role of histone acetylation in the regulation of the chromatin structure, differentiation, and the cell cycle."

An Examiner is not free to pick and choose selected sentences from a reference, but rather must consider the teaching of the reference as a whole. The quotes above are not the statements of an author motivating others to use antisense to inhibit histone deacetylase. Accordingly, Applicants respectfully reiterate that there is no motivation in the prior art to combine the cited references. Thus, Applicants respectfully request that the rejection of claims 1-3, 5 and 7 for obviousness be withdrawn.

If the Examiner believes that any discussion of this reply would be helpful, the Examiner is invited to call the undersigned attorney by telephone at 781-933-6630.

Respectfully submitted,

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